Patients' experiences and views of cascade screening for familial hypercholesterolemia (FH)

J Community Genet (2011) 2:249–257
DOI 10.1007/s12687-011-0064-y

ORIGINAL ARTICLE

Patients' experiences and views of cascade screening for familial hypercholesterolemia (FH): a qualitative study

Nina Hallowell · Nick Jenkins · Margaret Douglas · Simon Walker · Robert Finnie · Mary Porteous · Julia Lawton

Received: 5 May 2011 / Accepted: 8 August 2011 / Published online: 2 September 2011

Abstract Familial DNA cascade screening for familial hypercholesterolemia (FH) has recently been introduced in Scotland. This study investigated index patients' experiences of DNA testing and mediating cascade screening. Thirty-eight patients with a clinical diagnosis of definite or possible FH who had undergone DNA testing in the lipid clinic took part in semi-structured qualitative interviews. All patients were positive about DNA screening being undertaken by familiar and trusted clinicians within the lipid clinic. Most patients had already cascaded close relatives for serum cholesterol testing following their attendance at the lipid clinic. Identified mutation carriers who had attended the genetics clinic (n=15) for a cascading appointment described finding this consultation helpful because it identified other at-risk family members and provided them with tailored information for their relatives. Participants who expressed a preference said they favoured indirect (patient-mediated) methods of cascading as they considered indirect approaches to be less threatening to family members than direct clinical contact. We conclude that DNA screening and indirect familial cascading is perceived as highly acceptable to index patients with FH. However, while indirect cascading methods may be more acceptable to patients, they do not yield the same numbers as more direct methods. There is, therefore, a need for further systematic research to investigate patients', family members' and staff views of the acceptability of direct versus indirect methods of cascade screening.

Keywords Familial hypercholesterolemia (FH) · Indirect cascade screening · Qualitative interviews

N. Hallowell (✉)
Institute of Health and Society,
Newcastle University,
Newcastle, UK
e-mail: Nina.Hallowell@ncl.ac.uk

N. Jenkins · J. Lawton
Centre for Population Health Studies,
University of Edinburgh,
Edinburgh, UK

M. Douglas
Public Health/Health Policy,
NHS Lothian,
Edinburgh, UK

S. Walker
Clinical Biochemistry, Division of Reproductive
and Developmental Sciences,
University of Edinburgh,
Edinburgh, UK

R. Finnie
St John's Hospital Livingston
and Edinburgh Royal Infirmary,
Edinburgh, UK

M. Porteous
Western General Hospital,
Edinburgh, UK

Introduction

Ten million people worldwide are at increased risk of cardiovascular disease and premature death because they carry a genetic mutation predisposing them to familial hypercholesterolemia (FH) (WHO 1998). FH is an autosomal dominant disease, which manifests as an increase in blood levels of low

density lipoprotein (LDL) cholesterol. The high atherogenic LDL cholesterol level is associated with an earlier than average onset of coronary events, and young people who have FH (<40 years) have a nearly 100 times increased risk of fatal heart attack (Neil et al. 2000; Marks et al. 2006). Clinical diagnosis is based upon a combination of physical and clinical features including: raised levels of LDL cholesterol, a significant family history of early onset cardiovascular disease, and the presence of tendon xanthomas (cholesterol deposits) (the Simon Broome Criteria (DeMott et al. 2008)). Early detection and treatment with statins can be effective in reducing morbidity and mortality in those with heterozygous FH (DeMott et al. 2008; Scientific Steering Committee 1999). The severity of FH's consequences and its treatability mean that screening for this is prioritised by the Department of Health in the UK (Department of Health 2003). However, increasing the sensitivity and specificity of diagnosis of FH requires use of DNA testing (Humphries et al. 2006; Minhas et al. 2009). DNA screening facilitates diagnosis of younger pre-symptomatic patients and children in particular (Civeira et al. 2008; Finnie 2010). DNA testing in combination with familial cascade screening is seen as a very cost-effective way of reducing premature death from cardiovascular disease (Marks et al. 2002; Finnie 2010). Familial cascade DNA screening is now a clinical reality in Spain (Civeira et al. 2008), Norway (Leren 2004), the Netherlands, Scotland and Wales and has been recommended in England (DeMott et al. 2008; NICE 2008).

The question of whether cascading should be direct (i.e. involve direct contact from the clinic using either telephone calls or letters) or indirect (i.e. mediated by patients who pass on personalised clinic letters/information) raises a number of ethical dilemmas, for example, “maximising the utility of cascade screening” versus respecting probands' and relatives' privacy and preventing bodily harm in relatives versus causing psychological harm by undermining relatives' right to not know information (Newson and Humphries 2005 p. 402). Newson and Humphries (2005) argue that while direct approaches to FH cascading can be defended on ethical grounds, in practice, it would be advisable to involve the proband in the process if possible.

Direct FH cascading screening has recently been trialled in the UK (Hadfield et al. 2009); in line with findings from an earlier review of the Dutch FH programme (Umans-Eckenhausen et al. 2001), it was found that systematic family tracing by trained personnel plus direct clinical contact results in significantly more relatives coming forward for cholesterol screening (Hadfield et al. 2009). Direct approaches have also been supported on the grounds that they may help overcome patients' reticence to disclose/distribute information (Suthers et al. 2006) and thus maximise the number of relatives approached and captured in the cascade. However, research suggests that family communication about genetic testing usually takes place without need for this form of intervention, although the timing of disclosure may be influenced by social, emotional and contextual factors (Hallowell 2003). Furthermore, direct familial cascading is reliant upon index patients revealing family contact details, and this may raise issues about confidentiality for some individuals who may prefer to control the cascading of information in their family (Hallowell et al. 2003; Horstman and Smand 2008). Finally, indirect contact could be a more cost-effective option as it saves training and employing specialist staff to trace and contact relatives.

While questions have been raised about the most efficient way of implementing familial cascading for FH (Marteau et al. 2004; Minhas et al. 2009), limited attention has been paid to index patients' preferences for different cascading methods. Some research suggests that direct cascading is perceived as acceptable to members of the public (Tonstad et al. 1995) and family members (van Maarle et al. 2001). However, the former study asked about a hypothetical scenario (Tonstad et al 1995), and the latter only assessed the views of first- and second-degree relatives who had been captured by the cascade, rather than those initiating the process (van Maarle et al. 2001). Recent research in the Netherlands has looked at the role played by index patients in distributing generic information packages about FH in families (van den Nieuwenhoff et al. 2006). This study found that index patients preferred to distribute packages during face–face meetings with close (usually first-degree) relatives, but were ambivalent about distributing them to more distant relatives. To date, no research has looked at the views of index patients who are involved in initiating or mediating a familial cascade. Hence, it is not known whether indirect approaches are acceptable to patients and whether they raise any practical or ethical concerns. This paper looks at patients' experience of undergoing DNA testing in the lipid clinic, their subsequent referral to clinical genetics for family tracing and their views on having to mediate familial cascade screening. The objective is to guide and inform the development of future cascade screening programmes (Pedersen et al. 2010).

Methods

This study was undertaken in the Lothian region of Scotland where diagnostic DNA screening targeted at individuals who met the Simon Broome criteria for the diagnosis of FH has been ongoing since November 2008.

The cascading screening service in this region is detailed in Box 1. The South East Scotland Ethics Committee approved the study (ref: 09/S1102/66) in January 2010. In-depth interviews were conducted with index patients who had participated in DNA screening and familial cascading consultations. This qualitative design enabled patients to display their own understandings and experiences of DNA screening and familial cascading and to raise issues they perceived as most important. To contextualise the study and enable familiarisation with the DNA screening process, NJ and NH conducted observations of a series of consultations in two lipid clinics and a clinical genetics department, and NJ interviewed eight healthcare providers associated with these clinics (see Box 1).

Scottish patients who have a diagnosis of possible FH are referred from general practice, or other hospital departments, for treatment in specialist lipid clinics. Since the introduction of DNA testing in 2008, all new and returning lipid clinic patients provide blood samples for the purposes of genetic testing during their review appointment. These samples are taken at the same time as samples for routine biochemical analyses. In one of the clinics (Clinic A) we observed these were taken prior to patients seeing the Doctor. During the consultation the Doctor asks those patients who have not had DNA testing for their consent to have the blood sample taken, or sent, for DNA analysis. The patient consents or refuses.

If a genetic mutation associated with FH is not identified in a patient's sample, they receive a letter informing them of this and remain under the care of the lipid clinic, with a clinical diagnosis of probable FH. They are advised in this letter to encourage other family members to seek cholesterol screening, for example, Clinic A advises patients to "… speak to close family members with a view to each person obtaining a fasted, full lipid profile through their own GP." (clinic letter 2010). Those who are mutation positive receive written confirmation that they have a specific genetic mutation associated with FH and a referral to clinical genetics so that they may discuss their results and identify family members for cascade screening.

During the genetics consultation a detailed pedigree is drawn and at-risk relatives are identified. This clinical service has adopted an indirect method of familial cascading - the genetics staff offer to provide letters and written material for the patient to send/give to at-risk family members. Thus, the cascade process in this case is dependent upon family communication and the patients' willingness to pass on information.

Patients who carry FH mutations and have a definite diagnosis of FH will be followed up at least annually at the lipid clinic on an indefinite basis. This is in accordance with NICE guidelines, which recommend a yearly assessment in a specialist clinic. Patients who receive an inconclusive result will continue to attend the lipid clinic on an annual basis. Those family members who receive a negative predictive test result will not need to be referred to the lipid clinic and will be discharged from clinical genetics.

Box 1: The process of DNA screening and familial cascading in these clinics

Sampling and recruitment

Patients who had undergone DNA screening were recruited between May–December 2010. One hundred and fourteen patients who had undergone DNA screening and one patient who declined testing (total $n=115$) were contacted by letter and/or face-to-face by lipid clinic staff. Each patient received an information sheet outlining the study, an expression of interest form and a stamped addressed envelope. Patients were asked to return the expression of interest form directly to the researchers.

Data collection and analysis

Interviews were conducted by NJ at a time and location (e.g. patient's home/university offices) chosen by participants.

With one exception, all interviews were carried out face–face. Interviews were informed by a topic guide, developed following clinic observations and informal interviews with staff and modified in the light of emerging findings. Interviews explored patients': experiences of attending the lipid clinic and clinical genetics (if appropriate); understandings of FH and its treatment; and perceptions and experiences of genetic testing, obtaining and interpreting DNA results and communicating results within the family. Interviews were digitally recorded (with consent) and transcribed in full.

Data collection and analysis were concurrent, and interviews were analysed using the method of constant comparison (Strauss and Corbin 1990). Interview transcripts were reviewed by team members and systematically compared in order to identify cross-cutting themes and highlight common and divergent experiences between and within groups. Themes that emerged in early interviews were explored further in subsequent interviews, in line with an inductive approach. Data collection ceased when no new themes emerged. A coding frame was developed to capture data relating to emergent themes and the primary research aims. Data were managed using NVivo 8 (QSR International, VIC, Australia), a data-indexing package.

The sample

Forty three of the 115 (37%) patients who were approached opted into the study, and 38 (33%) were interviewed; the remaining patients were either excluded as they did not fit study criteria or were unavailable for interview. The majority (79%) were over 45 years of age. All had DNA testing, and 61% were identified as carriers of FH mutations. Fifteen patients (65%) with a positive DNA result had attended genetic counselling before the interview. (See Table 1.)

Table 1 Patient characteristics

	n (%)
Age (years) at interview	
Mean	52.63
Range	18–67
≤45 years	8 (21)
Gender	
Female/Male	21 (55):17 (45)
Education	
Compulsory education	14 (37)
Further education	4 (11)
Higher—HNC/HND	4 (11)
Higher—degree/postgraduate	16 (42)
Current/Most recent occupation	
Professional and managerial	11 (29)
Skilled non-manual	9 (24)
Semi-skilled non-manual	11 (29)
Skilled manual	2 (5)
Semi-skilled manual	1 (3)
Routine manual	2 (5)
Other/Unclassified	2 (5)
NHS/(Human) health sector (incl. clerical/admin)	7 (18)
NHS/(Human) health sector (excl. clerical/admin)	5 (13)
Mutation status	
Mutation identified/No mutation identified	23 (61):15 (39)
Clinical genetics	
Attended genetic counselling	15 (39)
Estimated years attending specialist lipid clinics	
0–2	11 (29)
3–4	7 (18)
5–9	7 (18)
10+	13 (34)

Results

Patients' views of DNA screening in the lipid clinic

All patients talked about valuing the care received in the lipid clinic, describing the staff who worked there as: “very charming” (FH11), having a good “bedside or desk-side manner” (FH12) and as “absolutely fantastic” (FH17). Many patients had been attending the same lipid clinic for many years and commented upon the importance of continuity of care for engendering a trusting relationship with staff: “I actually quite like it because I know I am getting looked after and I'll do anything to help them as well because they have been so good to me over the years trying different thing.” (FH25).

Patients were overwhelmingly positive about DNA screening, primarily because they saw it as an opportunity to confirm that the tendency towards high cholesterol in themselves and their family was inherited. Many noted that the routinised nature of phlebotomy in the lipid clinic meant that DNA testing appeared to be fully integrated into standard clinic procedures and, therefore, was considered neither onerous nor a significant event (FH12, Box 2). As FH36 said, “I didn't consider it, if you like, to be a DNA test or a genetic test in the sense that it just followed naturally through”. Indeed, a couple of patients suggested that, had DNA testing required other, or additional, procedures (e.g. buccal swabs), they might have thought more before consenting to this procedure (FH07, Box 2).

DNA screening in the lipid clinic

FH12: It was completely innocuous so, you know, you got another phial of blood taken and it was sent off to a lab. I've no idea what they did with it.

FH07 I guess if they'd taken a hair sample or a mouth swab, something different, then that might have had a more impactive feeling for me but it was just what normally goes on there, a bit more blood, cool.

I: how do you feel about the way the genetic test was carried out?

FH42: It was absolutely seamless for me and I had the bloods taken at the clinic which would have been taken anyway at the beginning of the cardiology appointment. ..it was hassle-free and it was excellent, …I was notified as soon as they got the results... It was handled really well, really professionally...

FH09: I almost feel that there was too much fuss about it. It really almost should have been, you know, throw all the rest of it to one side, it's a test that you could benefit from, take the test and there you are.

Clinical genetics consultations

FH05 then showed me exactly, from the wee diagram, how it can work... it was the use of the arrows explaining how I could have it and then…But it was just a wee diagram that she had and it was really when you put it all together and you look at it you're like "uh, the odds don't look good!"

FH24 I think it was quite good the meeting …because I don't think, if I'd been told, okay you've got the genetic I don't think I would have probably taken it further than, than myself. *(I: right. So, having that session led to think about other family members?)*…Yeah, because I probably would nae have thought. As I say, it would have come down to the fact, I was thinking, I don't have any children, it doesn't matter. I wasn't thinking extended [family]

FH35 … it was short, just basically asking us and she sort of drew a little picture of the family tree thing coming down like that and basically asked, you know, from my parents to me to [name of daughter] to grandkids, blah, blah, blah, my brothers, my sisters, and that went quite well and she sent me out the information to pass on to them, which I've done.

FH02 …it put in writing what the doctor had explained and, you know, for a non-medical person it's sometimes difficult to… you think you're following something when it's being explained to you but then afterwards you're a little bit confused and it's good to have it in writing.

FH03 'Cause they even sent a copy of the letters to my daughter, to one of my daughters and she gave them, I got copies for all of them and she gave them the copies.

FH34 Yeah well, we did pass on the letter and stuff to him [uncle]. Because we got the letter for him rather than it being posted out because we see him all the time, so we got the letter. So he was going to get checked. I think he maybe got checked before and didn't have it but he was going to get re-checked, since the genetics letter came out.

FH16 And I don't think that doctors or the health service should have to hold hands to people. Basically, we are adults and we are given information and if we don't deal with that or don't deal with our families, I think that's where the problem lies and not with the health service.

I: [is telling relatives] something which you would prefer hospital, NHS staff to do?

FH07 No, no, I would have liked to have done that "I've undertaken this test, this is what it's shown, that it's going to impact on you, here you are", rather than a letter from... a Data Protection... bland, redacted note from the NHS saying "well, you may or may not actually have a genetic..." – "thanks very much!" It would have been better and more honest from me, that's how I would have played that.

FH05…it's better if you do it, you know, because getting a letter from a strange clinic that you know nothing of is... At least they know, when the letter comes out, it's coming from me, it's not coming from, you know, somebody without a face. And I can say to them, you know "this is what's happened and this is what you need to do." It's better coming from me, I think.

Box 2: Patients' views of DNA screening and cascading

As far as most patients were concerned, DNA testing was handled "professionally" and well by clinic staff (FH42, Box 2). However, a small number described the administration of the testing process as unnecessarily cautious (FH09, Box 2) given that they already perceived their high cholesterol to be familial in origin. While some patients commented that written notification of their results had taken a while to arrive, no concerns were raised about receiving DNA results in a letter rather than face–face.

Patients' views of cascade screening

With the exception of one patient who felt he had not learnt any new information during his genetics consultation, all those who attended the genetics clinics were overwhelmingly positive about their consultation. Patients explained that clinic attendance had provided opportunities to ask questions and receive answers about the aetiology and transmission of disease in their family (FH05, Box 2). Many patients also described the drawing up of a detailed pedigree as an important event which had emphasised and illuminated their family's risks in ways they had not previously considered (FH05, FH24; Box2). Seeing their family history committed to paper during the genetics consultation helped clarify where in the family FH may have come from and where it might go and, therefore, who needed to be informed. As FH24 said "…I was quite amazed that they were looking at cousins…" (See Box 2).

Many patients had come to believe or suspect that high cholesterol ran in their families prior to being approached to take part in DNA screening and had already discussed their condition with their relatives. Lipid clinic staff were described as having played a pivotal role in encouraging patients to think about their family members' risk, and some patients' comments indicated that lipid clinic staff had been "unofficially" initiating a cascade of family members for cholesterol screening over a number of years: "[Lipid consultant] was very clear that the family should take this seriously and have tests from time to time. I've conveyed that to them" (FH16). However, family history taking in these lipid clinics is not systematic, and the staff do not draw up detailed pedigrees of the whole family or undertake family tracing. Thus, when patients talked about who they had contacted following their lipid appointments, the majority reported only informing (emotionally and geographically) close kin, primarily, first- (children and siblings) and second-degree (nieces and nephews) relatives. A few, however, also said they had, or would, ask an intermediary (e.g. sister (FH36), parent (FH09, FH 34)) to relay information to more distant relatives.

The cascading process in the genetics clinic not only employed a more systematic approach to family history taking, but also provided patients with leaflets and personalised letters to forward to at-risk family members on the clinic's behalf (Box 1). With one exception, all those who had attended their cascade appointment appreciated the support received in disseminating information throughout their family. Patients liked being told who needed to receive information and being given written information to distribute to particular relatives rather than having to rely on memory (FH02, Box 2). Indeed, receiving letters/information to pass on to more distant relatives—those they saw less frequently or with whom they were not in contact—was perceived as particularly helpful. Most patients reported distributing the information throughout their family as instructed (e.g. FH03, FH35; Box 2) and, in some cases, that the clinic letters had already prompted family members to get tested (FH34, Box 2).

Most patients were happy to assume responsibility for disseminating information about cholesterol or genetic screening in their family: "…it's [communicating information] just something you have to do really, you know, it's a responsibility you have." (FH13, FH16; Box 2) When asked whether they would prefer to be involved in indirect or direct cascading, the majority expressed a preference for indirect methods: "Well, I would hate just for a letter to land on their doorstep saying "would you take part in this?" (FH37). Patients' accounts suggested that involving the patients themselves (or another family member) made the process more personalised and, therefore, potentially less threatening for relatives (FH07, FH05; Box 2).

Discussion

DNA cascade screening is increasingly becoming the preferred approach for identifying FH in asymptomatic individuals, within the UK and across Europe (Leren 2004; Finnie 2010); however, as Marteau et al. (2004) note, relatively little is known about the impact on participants, particularly those initiating the familial cascade. The recent introduction of DNA cascade screening for FH in Scotland, therefore, has provided an important and timely opportunity to explore index patients' views of this service. The data indicate that index patients, like family members reached by cascading in the Netherlands (van Maarle et al. 2001), viewed DNA testing and cascade screening positively.

In contrast to recent research, which suggests that lipid clinic patients rarely communicate about FH with family members (Weiner and Durrington 2008), this study, like earlier Dutch (van den Nieuwenhoff et al. 2007; Horstman and Smand 2008) and Welsh studies (McDowell et al. 2007), found that, when given appropriate information and support, patients do feel willing and able to talk about FH with relatives and will cascade first-(McDowell et al. 2007) and second (McDowell et al. 2007; van den Nieuwenhoff et al.

2007)-degree relatives for cholesterol screening or DNA testing. These differences may be due to the fact that patients in this study and these earlier studies (McDowell et al. 2007; van den Nieuwenhoff et al. 2007) obtained a molecular rather than just a clinical diagnosis of FH (Weiner and Durrington 2008). Indeed, authors of the Welsh study propose that having DNA testing may assist risk communication in some families. Our data suggest this may be due to patients attending genetic consultations, where systematic discussion of the family history during the drawing of the pedigree helps patients establish which members of the extended family are at risk and thus who would benefit from receiving screening information. Thus, cascading appointments with staff trained in family history taking may facilitate insight into the genetic transmission of FH and thus result in more communication with emotionally, geographically and biologically distant relatives. This is an important issue to consider as other studies suggest that many of those who have genetic testing for FH (van den Nieuwenhoff et al. 2006, 2007), or other genetic conditions (Hallowell 2003; Hallowell et al. 2003), may be unaware of the implications for the extended family. In addition, providing individuals with personalised materials to distribute to more distant (socially or biologically) family members was appreciated and perceived as aiding family communication. These observations suggest that, at least from the index patient's point of view, referral to clinical genetics for familial cascading is worthwhile. However, it must be noted that the fact that FH is not seen as a particularly debilitating or stigmatising genetic disease and is one which is easily treated (Jenkins et al., under review) may also increase patients' apparent willingness to disseminate information within their family.

Gauging index patients' preferences about the method of familial cascading is important given the continuing debate about whether clinicians should contact family members directly to disclose genetic information and inform them about the opportunity for predictive testing (Offit et al. 2004; Newson and Humphries 2005). Empirical research suggests that direct contact by a member of the clinical team maximises the numbers of family members coming forward for FH screening (Umans-Eckenhausen et al. 2001; Hadfield et al. 2009); however, it also raises ethical issues. For example, an earlier Dutch study of FH cascading reported that 20% of family members approached reported feeling under pressure to have DNA testing following direct clinical contact (van Maarle et al. 2001). The ethico-legal debate about disclosure of genetic information by clinicians frequently focuses upon breaches of confidentiality and patients' right to privacy versus family members' right to know genetic information about themselves and be informed about testing/treatment option (Newson and Humphries 2005; Leonard and Newson 2010; Skene and Forrest 2010). This study, like that reported by Horstman and Smand (2008), suggests that index patients may be less worried about their own and/or relatives' privacy than ensuring that their relatives are not made unduly anxious by unsolicited approaches from the clinical team. Thus, like those who undergo testing for other dominant disorders (Hallowell et al. 2003; Kohut et al. 2007), they feel they should bear the initial responsibility for disseminating information within their family (Horstman and Smand 2008). It must be noted, however, that while index patients hypothesised that their involvement in cascading may be appreciated, or preferred, by their relatives, no cascaded family members were interviewed in this study, although, as mentioned above, there is evidence to suggest that approaches from the clinical team are sometimes perceived as coercive (van Maarle et al. 2001) or as an invasion of privacy (Horstman and Smand 2008).

Policy and practice implications

This study lends support for the adoption of indirect methods of cascading for FH, by highlighting the value that patients placed on having a systematic family history taken and being given letters for distribution to relatives, to help them communicate genetic information within their family. However, it must be noted that the advantages of employing an indirect approach may be offset by reduced uptake of screening amongst relatives (Umans-Eckenhausen et al. 2001; Hadfield et al. 2009). A compromise position might, therefore, be to encourage index patients to contact family members in the first instance, thereby allowing them to discharge their familial obligations and then follow this up, if required, by direct contact from a healthcare worker (Newson and Humphries 2005). These observations suggest more systematic research is needed to compare index patients' and family members' experiences of the different methods of familial cascading employed in this and other studies, as well as the (cost-) effectiveness of each approach.

Strengths and limitations

This is the first study to explore in-depth index patients' views and experiences of mediating a familial cascade for FH. When interpreting these findings, it must be noted that this study included a small, highly educated sample, a sizeable proportion of whom had previously worked in health-related occupations, who were the first patients in Scotland to be offered this type of test, and that these factors may have influenced their willingness to participate, as well as their understandings and views. Similar participant characteristics have been observed in other qualitative studies involving FH patients attending lipid clinics (Weiner 2006). This may be due to the fact that lipid clinic patients are not necessarily

representative of the wider FH population, as fewer than 20% of all FH patients may be receiving care in specialist lipid clinics, which are predominantly located in urban areas (Marks et al. 2004). As a retrospective design was used, it is possible that patients' accounts may have been subject to recall bias. Moreover, as patients opted in to the study, it is possible that those who had more extreme views participated. Indeed, over 60% of the sample had received a positive DNA test result, whereas the detection rate for known mutations in Scotland for 2009–2010 was 29.3% (Bell 2010). We can speculate that those who received an inconclusive result may not have felt as motivated to take part as it was clear that testing was not perceived as such a significant event for this group (Jenkins et al., under review). Finally, it is possible that the patients in this study may have been positive about indirect methods of cascading because this is the method they are familiar with. Indeed, it has been observed that patients appear to favour the services they receive (Porter and Macintyre 1984). This may be the case; however, it should be noted that a couple of patients who received inconclusive results and had not been involved in the official cascade also expressed a preference for indirect methods.

Acknowledgements We would like to thank all the patients who took part in the study and the staff at all of the clinics that participated, in particular Katriona White, Suzanne McKenzie and Tricia Livani, who were involved in patient recruitment. In addition, we would like to thank Lisa Horsburgh, Lesley Gardner, Rosa Bisset and Terry Lisle whose secretarial and administrative skills were invaluable to the successful running of the project. This research was funded by a grant to NH, MD and JL from the Chief Scientists Office.

Conflicts of interest None declared.

Ethics approval Approval for the study was granted by the South East Scotland Ethics Committee (ref: 09/S1102/66) in January 2010.

References

Bell C (2010) Familial hypercholesterolemia testing in Scotland. Presented at the Scottish Lipid Forum. Dunkeld, 2010

Civeira F, Ros E, Jarauta E, Plana N, Zambon D, Puzo J et al (2008) Comparison of genetic versus clinical diagnosis in familial hypercholesterolemia. Am J Cardiol 102:1187–1193

DeMott K, Nherera L, Shaw EJ, Minhas R, Humphries SE, Kathoria M et al (2008) Clinical guidelines and evidence review for familial hypercholesterolaemia: the identification and management of adults and children with familial hypercholesterolaemia. National Collaborating Centre for Primary Care and Royal College of General Practitioners, London

Department of Health (2003) Our inheritance our Future. HMSO, London

Finnie RM (2010) Cascade screening for familial hypercholesterolaemia in Scotland. B J Diabetes & Vasc Dis 10:123. doi:10.1177/1474651409343245 accessed 23/11/2011

Hadfield SG, Horara S, Starr BJ, Yazdgerdi S, Marks D, Bhatnagar D et al (2009) Family tracing to identify patients with familial hypercholesterolaemia: the second audit of the Department of Health Familial Hypercholesterolaemia Cascade Testing Project. Ann Clin Biochem 46:24–32. doi:10.1258/acb.2008.008094

Hallowell N (2003) Ethics and evidence. In: Cooper DN (ed) The encyclopedia of the human genome. Nature Publishing Group, London

Hallowell N, Foster C, Eeles R, Ardern-Jones A, Murday V, Watson M (2003) Balancing autonomy and responsibility: the ethics of generating and disclosing genetic information. J Med Ethics 29:74–79

Horstman K, Smand C (2008) Detecting familial hypercholesterolaemia: escaping the family history? In: de Vries G, Horstman K (eds) Genetics from the Laboratory to Society: societal learning as an alternative to regulation. Palgrave Macmillan, Basingstoke, pp 90–117

Humphries SE, Cranston T, Allen M, Middleton-Price H, Fernandez MC, Senior V, Hawe E, Iversen A, Wray R, Crook MA et al (2006) Mutational analysis in UK patients with a clinical diagnosis of familial hypercholesterolaemia. J Mol Med 84:203–214

Kohut K, Manno M, Gallinger S, Esplen MJ (2007) Should healthcare providers have a duty to warn family members of individuals with a HNPCC-causing mutation? A survey of patients from the Ontario Familial Colon Cancer Registry. J Med Genet 44:404–407

Tonstad S, Vollebaek LE, Ose L (1995) Screening for familial hypercholesterolaemia in relatives. Lancet 346:1438

Leonard SJ, Newson AJ (2010) Ethical perspectives. In: Gaff CL, Bylund CL (eds) Family communication about genetics. OUP, Oxford, pp 199–214

Leren TP (2004) Cascade genetic screening for familial hypercholesterolemia. Clin Genet 66:483–487

Marks D, Wonderling D, Thorogood M, Lambert H, Humphries SE, Neil HA (2002) Cost effectiveness analysis of different approaches of screening for familial hypercholesterolaemia. BMJ 324(7349):1303

Marks D, Thorogood M, Farrer JM, Humphries SE (2004) Census of clinics providing specialist lipid services in the United Kingdom. J Pub Health 26(4):353–354

Marks D, Thorogood M, Neil SM, Humphries SE, Neil HAW (2006) Cascade screening for familial hypercholesterolemia. J Med Screen 13:156–159

Marteau T, Senior V, Humphries SE, Bobrow M, Cranston T, Crook MA et al (2004) Psychological impact of genetic testing for familial hypercholesterolemia within a previously aware population: a randomized controlled trial. Am J Med Genet A 128A:285–293

McDowell I, Watson M, Townsend D, Featherstone K, Parham K, Whatley S (2007) An evaluation of DNA diagnostics for familial hypercholesterolaemia including a study of personal and family implications. Atherosclerosis 194:282

Minhas R, Humphries SE, Qureshi N et al (2009) Controversies in FH: a commentary on the NICE guideline for the identification and management of familial hypercholesterolemia. Heart. doi:10.1136/hrt.2008.162909 accessed 13 10.2010

Neil HAW, Hammond T, Huxley R, Matthews DR, Humphries SE (2000) Extent of under diagnosis of familial hypercholesterolaemia in routine practice: prospective registry study. BMJ 321:148–149

Newson AJ, Humphries SE (2005) Cascade testing in familial hypercholesterolaemia: how should family members be contacted. Eur J Hum Genet 13:401–408

NICE (2008) Identification and management of familial hypercholesterolemia CG71 familial hypercholesterolemia: NICE Guidelines http://www.nice.org.uk/Guidance/CG71/NiceGuidance/pdf/English. Accessed 21/02/09

Offit K, Groeger E, Turner S, Wadsworth EA, Weister MA (2004) The "Duty to Warn" a patients family members about hereditary disease risks. JAMA 292:1469–1473

Pedersen KMV, Humphries SE, Roughton M, Besford JS (2010) National clinical audit of the management of familial hypercholesterolaemia full report. Clinical Standards Department, Royal College of Physicians

Porter M, Macintyre S (1984) What is must be best: a research note on conservative or deferential responses to antenatal care provision. Soc Sci Med 19:1197–1200

Scientific Steering Committee, of Simon Broome Register Group (1999) Mortality in treated heterozygous familial hypercholesterolaemia: implications for clinical management. Atherosclerosis 142:105–112

Skene L, Forrest L (2010) Legal perspectives. In: Gaff CL, Bylund CL (eds) Family communication about genetics. OUP, Oxford, pp 215–226

Strauss A, Corbin J (1990) Basics of qualitative research. Sage, London

Suthers G, Armstrong J, McCormack J, Trott D (2006) Letting the family know: balancing ethics and effectiveness when notifying relatives about genetic testing for a familial disorder. J Med Genet 43:665–670

Umans-Eckenhausen MAW, Defesche JC, Sijbrands EJG, Scheerder RLJM, John JP, Kastelein JJP (2001) Review of first 5 years of screening for familial hypercholesterolaemia in the Netherlands. Lancet 357:165–168

van den Nieuwenhoff L et al (2006) The importance of written information packages in support of case-finding within families at risk for inherited high cholesterol. J Gen Couns 15(1):29–40

van den Nieuwenhoff L et al (2007) Family communication regarding inherited high cholesterol: a qualitative social ecological approach. Soc Sci Med 65(55):1025–1037

van Maarle MC, Stouthard MEA, Marang-van de Mheen PJ, Klazinga NS, Bonsel GJ (2001) How disturbing is it to be approached for a genetic cascade screening programme for familial hypercholesterolaemia? psychological impact and screenees'. Views Com Gen 4:244–252

Weiner K (2006) Patient and professional constructions of familial hypercholesterolaemia and heart disease: testing the limits of the geneticisation thesis. PhD thesis, University of Nottingham

Weiner K, Durrington PN (2008) Patients' understandings and experiences of familial hypercholesterolemia. Community Genet 11(5):273–282

World Health Organisation (1998) Familial hypercholesterolaemia (FH). WHO, Geneva